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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,294	11/17/2000	Narendra S. Yadav	CL1127 US CIP1	5868

23906 7590 02/17/2004

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EXAMINER

MEHTA, ASHWIN D

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 02/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/715,294

Applicant(s)

YADAV, NARENDRA S.

Examiner

Ashwin Mehta

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-43, 70 and 80-86 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-43, 70, and 80-86 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 1/13/2003 & 2/3/2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The rejection of claims 82, 84, and 86 under 35 U.S.C. 112, 1st paragraph, is withdrawn and replaced with the rejection below.

Continued Examination Under 37 CFR 1.114

3. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on November 20, 2003 has been entered.

Claim Objections

4. Claims 41, 82, 84, and 86 are objected to because of the following informalities:

In claim 41: the claim is missing the period punctuation mark.

In claims 82, 84, and 86: in part 1)c)(iv) of the claims, in line 2, the semi-colon following "group consisting of" should be deleted or replaced with a colon.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. Claims 82, 84, 86, and 43 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 82, 84, and 86: the claims indicate that P2 is a “second floral specific promoter”. However, the claims subsequently indicate, in the last step of the methods, that P2 is activated in common germline. This renders the claims indefinite, as the claims have two different limitations for the P2 promoter.

6. Claims 39-43, 70, and 80-86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn towards a method for conditionally activating a transgene in a plant comprising 1) providing a construct comprising a first recombinase element having a promoter, P1, operably linked to a recombinase, R1, a second recombinase element comprising the general structure P2-RS1-STP-RS1-R2, a third recombinase element having the general structure P3-RS2-STP-RS2-TG, and a fourth recombinase element having the general structure P4-RS2-STP-RS2-TG2, wherein transgenic plants are provided that comprise two of the four recombinase elements, crossing the plants, wherein conditional expression of R1 from P1 is the common germline of a first generation plant and excises the STP fragment from the second

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recombinase element, activating P2 to express R2, wherein R2 excises the STP fragment from the third and fourth recombinase elements, allowing expression of the transgenes in the second generation; or a method for the conditional expression of a transgene in a plant comprising providing a multiplicity of recombinase elements; or a trait expression constructing comprising a first and second recombinase elements; or a method for conditionally activating a transgene in a plant, comprising the use of three recombinase elements, wherein the transgene expresses in the first and all subsequent generations of plants; or a method for conditionally activating a transgene in a second generation plant.

The specification teaches combinations of two site-directed recombination systems to cause developmentally staggered site-specific recombinations to control expression of a transgene in a plant. One of the recombinases would remove a stop or blocking fragment that lies between a second recombinase-encoding gene and its promoter. The two recombinases can be expressed at different points in plant development. The second recombinase can then remove a stop fragment located in between a transgene and its promoter. The specification indicates that the salient feature is that expression of the second recombinase or the transgene does not have to occur immediately upon removal of the stop fragment, but is controlled by the choice of the promoters (page 35, line 4 to page 36, line 30).

The claimed invention requires the use of multiple site-directed recombination (SSR) systems together in plants. However, the specification does not teach that multiple site-directed recombination systems can be used together in the same plant. The specification does not contain any working examples that demonstrate the claimed methods. While the prior art has numerous publications that teach the use of various site-specific recombination systems in plants,

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it is not clear that multiple systems can be used in plants together. Applicant states that the level of predictability for the function of several independent SSR systems in one or more plants is low and one of skill in the art could not a priori predict with any reasonable certainty that combinations of these systems would indeed work, that one of skill in the art would not have had a reasonable expectation of success given the state of the art (response submitted September 9, 2003, page 12, 4th full paragraph). Applicant has also stated that expression of certain recombinases are toxic to some tissues resulting in poor or no expression of the recombinases, and cite Heidmann et al. (Development Genes and Evolution (2001), Volume 211(8-9), pages 458-465) and Silver et al. (Cell (2001), Vol. 841, pages 233-243) in support, and admit that it was unclear at the time the invention was made what effect the expression of several different SSR elements in multiple tissues would have on plant metabolism (response submitted September 9, 2003, page 13, last paragraph; response submitted November 20, 2003, page 12, 4th paragraph). The instant specification does not teach how one skilled in the art is to overcome this problem of the art, and the instant specification does not contain any working examples that demonstrate that Applicant was successful in overcoming this problem, or what steps one skilled in the art should take to overcome the problem, which Applicant admits existed in the art at the time the application was filed. In the absence of further guidance, undue experimentation would be required by one skilled in the art to use multiple site-directed recombination systems in plants to activate a transgene, in the first, second, or subsequent generations. See Genentech, Inc. v. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that “the specification, not the knowledge of one skilled in the art” must supply the enabling aspects of the invention. Given the breadth of the claims, unpredictability of the art and lack of guidance of the

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specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 103

7. Claims 39-41, 70, 80, 81, 83, and 85 remain and claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Odell et al. "A" (Mol. Gen. Genet., 1990, Vol., 223, pages 369-378) in combination with Lloyd et al. (Mol. Gen. Genet., 1994, Vol. 242, pages 653-657), Applicant's admitted state of the prior art, and Odell et al. "B" (Use of Site-Specific Recombination Systems in Plants, in Homologous Recombination and Gene Silencing in Plants, 1994, pages 219-270, Ed. Paszkowski, J., Publisher: Kluwer, Dordrecht, Germany), for the reasons of record stated in the previous Office actions. Applicant traverses the rejection in the paper submitted November 20, 2003. Applicant's arguments have been fully considered but were not found persuasive.

Applicant again argues that the level of predictability for the function of several independent SSR systems is low and one of skill in the art in the art could not a priori predict with any reasonable certainty that combinations of these systems would indeed work (response, page 12, 4th full paragraph). The Examiner maintains that the cited references demonstrate that more than one site-specific recombinase system is active in plants. Odell et al. B also assert that the ability of site-specific recombinases to locate their target sites on individual chromosomes is quite impressive (page 260). Given these teachings, one of ordinary skill in the art had a reasonable expectation of success that two different site-specific recombination systems can work in the same plant without interfering with each other. Applicants again argue that the

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expression of multiple SSR systems in plants in multiple tissues has not been demonstrated prior to Applicant's invention (response, page 12, 4th full paragraph). However, Applicants do not show that others in the art tried and failed to simultaneously use multiple SSR systems in plants. It is also again noted that the instant specification does not demonstrate the claimed method in working examples. Applicant's claimed invention is not based on experimental results.

Applicant acknowledges that the expression systems in the references cited previously (in the response submitted September 9, 2003) are in *Drosophila* and mammalian tissue, but argue that the references are relevant to support the notion of unpredictability in plant cells, (response, page 12, 5th full paragraph). However, Applicant does not explain why.

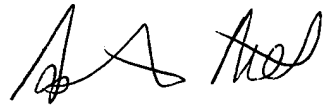
Applicant also argues that the prior art does not provide for embodiments of claims 81-86, which require the expression of a P3 driven transgene in a second generation plant, and argue that the combination of specific promoters required for transgene expression in second generation plants is not suggested or anticipated in the prior art (response, page 12, last paragraph). However, the methods of claims 81, 83, and 85 do not limit the type of promoters that can be used. Nor do those claims indicate that transgene expression fails to occur in the first generation. In fact, the last lines of claims 81, 83, and 85 indicate that transgene expression occurs in the first and all subsequent generations of plants.

8. Claims 39-43, 70, and 80-86 are rejected.

Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 571-272-0803. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

February 2, 2004



Ashwin D. Mehta, Ph.D.
Primary Examiner
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